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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/344,382	06/25/1999	SHUNICHI SOMA	050499/0101	9000

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EXAMINER	
ROMEO, DAVID S	
ART UNIT	**PAPER NUMBER**
1647	21

DATE MAILED: 01/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/344,382	SOMA ET AL.	
	Examin r	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-42 and 44-51* is/are pending in the application.

4a) Of the above claim(s) *22-28 and 44-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-28,45 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *22-42 and 44-51* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *20* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The request filed on October 31, 2002 (Paper No. 17) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09344382 is acceptable and a CPA has been established. An action on the CPA follows.

The preliminary amendment filed October 31, 2002 (Paper No. 18) has been entered. Claims 22-42, 44-51 are pending. Claims 29-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 4. Applicant's elected group I and the species that encompass continuous, systemic administration of PTH(1-34) in Paper No. 12. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 22-28, 44-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to, or to the extent that they are drawn to, a nonelected invention and/or species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 12. Claims 22-28, 45, 49, 50, 51 are being examined to the extent that they read upon the elected invention and/or species.

Claim Rejections - 35 USC § 103

Claims 22-28, 45, 49, 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gianelly (w6) in view of Kronenberg (A1, cited by Applicants), Gardella (A7, cited by Applicants), and Sindrey (A2, cited by Applicants) and further in view of Yamasaki (A5, cited

by Applicants), Collins (A19, cited by Applicants), Kamata (A6, cited by Applicants), Chao (A20, cited by Applicants), and Tam (a21).

Gianelly teaches that it appears possible to enhance orthodontic tooth movement by the local use of parathyroid hormone (page 305, full paragraph 4). Gianelly is silent with respect to PTH(1-84) and PTH(1-34) and the purity thereof.

Kronenberg teaches human PTH(1-84) and synthetic PTH(1-34) (column 9, line 55, through column 10, line 14; Figures 1-6). Human PTH(1-84) comprises amino acids 1 to 34, as recited in claim 26.

Gardella teaches hPTH(1-34) (Page 15858, Experimental Procedures, column 1, full paragraph 1), which is interpreted to mean human PTH(1-34).

The term "recombinant" in claims 25, 28 is a product-by-process limitation. A process limitation is not viewed as positively limiting the PTH absent a showing that the recombinant process of making PTH imparts a novel or unexpected property to the PTH.

Sindrey teaches the purification of PTH (page 7, lines 8-43).

Kronenberg, Gardella, and Sindrey do not teach enhancing orthodontic tooth movement by the local use of parathyroid hormone. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to enhance orthodontic tooth movement by the local use of parathyroid hormone, as taught by Gianelly, and to modify that teaching by using purified, human PTH(1-84) or PTH(1-34), as taught by Kronenberg, Gardella, and Sindrey, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings because Kronenberg, Gardella, and Sindrey provide a convenient source of readily purified PTH.

Gianelly in view of Kronenberg, Gardella, and Sindrey are silent with respect to administering PTH continuously in order to increase tooth movement in a subject in need thereof.

Yamasaki teaches that stimulation of osteoclastic activities and the resultant bone resorption are involved in orthodontic tooth movement (Figure 7).

Collins teaches that although various orthodontic appliances may differ in their mode of action they all must ultimately achieve the same effect - namely, the resorption and apposition of alveolar bone to produce tooth movement in the desired direction (page 278, column 1, full paragraph 1), and suggest increasing the rate of alveolar resorption in order to increase tooth movement during orthodontic procedures (page 283, column 1, full paragraph 1).

It is well known that PTH increases osteoclast activity and promotes bone resorption. See Kamata, page 412, full paragraph 1. The number of osteoclasts appearing during tooth movement is related to the function of PTH activity. See Kamata, page 424, full paragraph 4.

Chao suggest activating alveolar bone resorption during orthodontic tooth movement a more rapid bone modeling and tooth movement could be achieved (Abstract, third paragraph; paragraph bridging pages 307-308).

It has also been observed that the end result of the administration of PTH on skeletal homeostasis depends on how the hormone is administered. For the same daily dose, the bone volume shows a dose dependent increase if the daily dose of the hormone is given as one single injection. However, when the same daily dose is administered by continuous infusion with a subcutaneous miniosmotic pump, the result is bone loss. See Tam, column 3, lines 45-53.

Yamasaki, Collins, Kamata, Chao, and Tam do not teach administering PTH continuously in order to increase tooth movement in a subject in need thereof. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to enhance orthodontic tooth movement by the local use of PTH(1-84) or PTH(1-34), as taught by Gianelly in view of Kronenberg, Gardella, and Sindrey, and to modify that teaching by administering the PTH continuously, as taught by Tam, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because stimulation of osteoclastic activities and the resultant bone resorption are involved in orthodontic tooth movement, although various orthodontic appliances may differ in their mode of action they all must ultimately achieve the same effect - namely, the resorption and apposition of alveolar bone to produce tooth movement in the desired direction, and increasing the rate of alveolar resorption would increase tooth movement during orthodontic procedures, PTH increases osteoclast activity and promotes bone resorption, the number of osteoclasts appearing during tooth movement is related to the function of PTH activity, activating alveolar bone resorption during orthodontic tooth movement could achieve a more rapid bone modeling and tooth movement, and when PTH is administered by continuous infusion the result is bone loss. The invention is prima facie obvious over the prior art.

Claims 22, 49, 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gianelly (w6) in view of Kronenberg (A1, cited by Applicants), Gardella (A7, cited by Applicants), and Sindrey (A2, cited by Applicants) and further in view of Yamasaki, Collins,

Kamata, Chao, and Tam (a21) as applied to claims 22, 49 above and further in view of Schluter (a13).

Gianelly in view of Kronenberg, Gardella, and Sindrey and further in view of Yamasaki, Collins, Kamata, Chao, and Tam as applied to claims 22, 49 above teach administering PTH continuously in order to increase tooth movement in a subject in need thereof. Gianelly in view of Kronenberg, Gardella, and Sindrey and further in view of Yamasaki, Collins, Kamata, Chao, and Tam as applied to claims 22, 49 do not teach administering PTH in a composition comprising PEG.

Schluter teaches pharmaceutical dosage unit forms for systemic (parenteral) administration of PTH, which are useful for the mitogenic and bone growth effect in mammals. The term "dosage unit form" as used in this specification and in the claims refers to physically discrete units suitable as unitary dosages for mammalian subjects, each unit containing a predetermined quantity of the essential active ingredient, i.e., a modified PTH, calculated to produce the desired effect in combination with the required pharmaceutical means which adapt said ingredient for systemic administration. Examples of dosage unit forms in accordance with this invention are sterile preparations in liquid vehicles for parenteral administration and sterile dry preparations for the extemporaneous preparation of sterile injectable preparations in a liquid vehicle. Carriers or vehicles include liquid polyethylene glycol. See paragraph bridging columns 11-12. Schluter does not teach systemic administration of PTH in a preparation comprising PEG that results in tooth movement in a subject in need thereof.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer PTH continuously in order to increase tooth movement in a

subject in need thereof., as taught by Gianelly in view of Kronenberg, Gardella, and Sindrey and further in view of Yamasaki, Collins, Kamata, Chao, and Tam as applied to claims 22, 49 above, and to modify that teaching by systemic (parenteral) administration of PTH in a preparation comprising PEG, as taught by Schluter, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings in order to produce the desired effect (assist orthodontic tooth movement) in combination with the required pharmaceutical means (PEG) which adapt PTH for systemic administration. The invention is prima facie obvious over the prior art.

Response to Arguments

Applicants argue that continuous injection of PTH is superior to intermittent injection of PTH and that it was unknown that continuous infusion of PTH might be different from single or intermittent injection of PTH. Applicant's arguments have been fully considered but they are not persuasive. The prior art of record clearly recognizes that bone loss or resorption is associated with enhanced tooth movement and that continuous infusion of PTH results in bone loss, whereas bone volume increases if the daily dose of the hormone is given as one single injection. The differences between the prior art and the present invention are neither non-obvious nor unexpected.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

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DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
JANUARY 23, 2003